Psychemedics RIA Methamphetamine and MDMA Assay

1-24-02

510(k) SUMMARY [K011185]

I. General Information

A.	Submitter's Name:	Psychemedics Corporation
	Address:	5832 Uplander Way, Culver City, California 90230
	Telephone Number:	(310) 216-7776; (800) 522-7424
	Contact Person:	William R. Thistle, JD
	Date prepared:	26 October 2001
B.	Device Generic Name:	Analytical Service: RIA Methamphetamine and MDMA Assay
	Proprietary Name:	Psychemedics RIA Methamphetamine and MDMA Assay
	Classification Name:	91 (Toxicology) **cfr 862.3650**

Product Codes of Devices to Which Equivalence is Claimed: Dade Behring (K993982)

II. Intended Use

The Psychemedics Methamphetamine and MDMA Assay is a radioimmunoassay (RIA) for the qualitative and semi-quantitative detection of d-methamphetamine, d,l-MDMA and metabolites in hair samples at concentrations at or above 5 ng/10 mg hair for the purpose of identifying methamphetamine or MDMA (Ecstasy) use. This product is intended exclusively for in-house professional use only. The test is not intended for over the counter sale to non-professionals.

The Psychemedics Methamphetamine and MDMA Assay provides only a preliminary analytical test result. To confirm a screen positive result, a more specific alternate chemical method, such as LC/MS/MS, must be used. Clinical consideration and professional judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are obtained.

III. Description of the Product

The Psychemedics RIA Methamphetamine and MDMA Assay is based upon the competitive binding of ^{125}I-radiolabeled methamphetamine and unlabeled methamphetamine, MDMA and their metabolites, in proportion to their relative concentrations in the reaction mixture. An aliquot of a solution of enzymatically digested hair is added to a test tube with a fixed amount of radiolabeled methamphetamine, primary antibody (antiserum against methamphetamine), and second antibody. Following incubation, the mixture is centrifuged in the presence of polyethylene glycol, and the unbound fraction is discarded by decanting the supernatants of the precipitated antigen-antibody complex. The pellets containing the bound antigen are counted in a gamma scintillation counter. For the screening assay, a B/Bo x 100 less than or equal to the B/Bo x 100 of the 5 ng methamphetamine/10 mg hair cut-off calibrator is indicative of the presence of methamphetamine and/or MDMA.

The urinalysis predicate device used in the present study was the Dade Behring EMIT system. A Substantial Equivalence Comparison of hair analysis with the predicate device is shown in Section VIII.

IV. Precautions and Warnings

This assay was designed for use with human hair. Positive screening results only indicate the presumptive presence of methamphetamine/MDMA, requiring additional analysis by mass spectrometry. The device was evaluated using primarily vertex head hair samples from a population of multiple drug abusers between the ages of 20 and 56 in treatment programs. The conclusions from several large population studies attributed no statistically significant effects from hair color on test results. Interpretation of results must take into account that hair concentrations can vary dependent on hair collection body site and other biological variables. Certain medications that contain methamphetamine or metabolites of methamphetamine may cause a positive result.

A negative screening test result does not necessarily rule out the possibility of methamphetamine/MDMA use during the previous 90 days, i.e. time of collection, frequency of use, dosage used and other factors may

influence results. It is not possible to document all possible concentration reduction effects due to treatments such as bleaching, straightening and dying, hair types, frequency of use variations, dosages and combinations thereof. Therefore, all possible factors that may reduce methamphetamine/MDMA to below cutoff within user populations have not been determined. There is a possibility that other substances and/or factors not listed above may interfere with the test and cause false results that cannot be confirmed by mass spectrometry, e.g. technical or procedural errors.

V. Alternative Practices and Procedures

Blood and urine specimens have figured prominently in efforts to monitor drug use. Problems with the analysis of these specimens relate to evasion by adulteration of the specimen or temporary abstention from drug use; the latter is facilitated by the rapid clearance of drugs from blood or urine, usually 2-3 days after last use. To adequately detect drug intake over extended periods with urine, it is necessary to collect many specimens at short intervals relative to the half lives of the drugs in the body. For illicit drugs this would require multiple samplings per week.

VI. Marketing History

The analytic service of detecting drugs in hair began with the 1986 founding of Psychemedics Corporation, a public company dedicated to hair analysis for drugs of abuse. As the world's first commercial hair testing laboratory for drugs of abuse, Psychemedics focused on workplace testing of the NIDA-5 drugs (amphetamines, marijuana, opiates, cocaine, and phencyclidine). Since its founding, Psychemedics has performed hair analysis on over 2 million individuals (10 million tests). Test results have routinely been upheld in the courts.

Psychemedics is a California clinical reference laboratory and is licensed under the terms of the Clinical Laboratories Improvement Act (CLIA) of 1988 to engage in interstate commerce for the purpose of performing clinical tests on human subjects (toxicology/drugs of abuse). Psychemedics is also licensed by numerous State licensing authorities.

VII. Potential Adverse Effects on Health

Not Applicable

VIII. Equivalence Comparison

	Dade Behring EMIT(K993982)	Psychemedics RIA Methamphetamine and MDMA Assay
Type of Product	Analytical Reagents	Analytical Service
Measured Analytes	Amphetamines	d-Methamphetamine and d,l-MDMA
Test Medium	Urine	Hair
Cut-off levels	1000 ng Methamphetamine/mL	5 ng equiv. methamphetamine/10 mg hair
Test System	Competitive Enzyme Immunoassay	Competitive Radioimmunoassay
Materials	Monoclonal antibody; enzyme-labeled methamphetamine; optical assay of enzyme substrate	Polyclonal primary antibody; isotopically labeled methamphetamine; double antibody precipitation
Indications for Use	Identify Methamphetamine Use	Identify Methamphetamine and MDMA Use
Target Population	Workplace; criminal justice; medical	Workplace; criminal justice; medical
Mass Spectrometry Confirmation	Yes	Yes

IX. SUMMARY OF ANALYTICAL STUDIES

1. Sample Preparation and Stability of Methamphetamine and MDMA

The hair sample preparation for the assay is a 2-hour, pH=9.5, enzymatic digestion of the hair. Under various pH conditions for three concentrations levels, the stability of methamphetamine and MDMA during the digestion procedures has been studied to determine the recovery rates.

	pH Value	% Recovery Methamphetamine	% Recovery MDMA
Digest - after 2 hours	9.5	99.7	92.0

2. Matrix Effects

Variations due to matrix effects among different hair samples were assessed by digestion and assay of 100 methamphetamine/MDMA negative hair samples. In a study where the mean of the negatives was near 100%B/B_0, and where an attempt was made to minimize cross-rector effects, the mean of the negatives was 99.9 B/B_0, with a S.D. of 3.6, %C.V. of 3.6 and the 95% confidence intervals of 99.17 to 100.58

Similarly, matrix effects at the cutoff were assessed by spiking the same negative hair samples with methamphetamine (5 ng/10 mg hair) or MDMA (3.75 ng/10 mg hair), digesting and assaying them. For methamphetamine, the mean $\%B/B_0$ of the spiked samples was 54.33, S.D. was 2.4, %C.V. was 4.42, and the 95% confidence intervals 53.85 to 54.80. For MDMA, the mean $\%B/B_0$ of the spiked samples was 54.17, S.D. was 2.35, %C.V. was 4.32, and the 95% confidence intervals 53.71 to 54.63.

3. Limit of Detection (LOD)

At 2.5 ng/10 mg hair, the lowest standard concentration for which precision data was generated, the mean ng/10 mg hair of 20 assays was 2.62, with a S.D. of 0.15 and %C.V. of 5.59. The 95% confidence intervals were 2.55 to 2.69.

4. Precision for Methamphetamine

a. Within-Run

The intra-assay analytical precision around the cut-off (5 ng/10 mg hair) was determined. 20 replicate hair samples each were spiked before digestion at + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration of 5 ng methamphetamine per 10 mg hair.

Intra-Assay Precision of the Device

Methamphetamine spiked Concentration	Mean (ng/10 mg hair)	SD (ng/10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/10 mg hair)	2.59	0.16	6.07	2.51	2.66
-25% of cutoff (3.75 ng/10 mg hair)	4.12	0.32	7.84	3.97	4.28
100% of cutoff (5.0 ng/10 mg hair)	5.24	0.40	7.67	5.05	5.43
+25% of cutoff (6.25 ng/10 mg hair)	6.47	0.47	7.21	6.26	6.69
+50% of cutoff (7.5 ng/10 mg hair)	7.49	0.67	8.90	7.17	7.80

b. Between-Run

Inter-assay precision around the cut-off concentration was determined among 20 different assays performed (2 per day) for 10 days. Prior to digestion, hair samples were spiked at each concentration of + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration (5 ng methamphetamine/10 mg hair).

Inter-Assay Precision of Device

Methamphetamine Concentration	Mean (ng/10 mg hair)	SD (ng/10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/10 mg hair)	2.62	0.15	5.59	2.55	2.69
-25% of cutoff (3.75 ng/10 mg hair)	3.76	0.25	6.74	3.64	3.65
100% of cutoff (5.0 ng/10 mg hair)	5.08	0.27	5.24	4.94	5.18
+25% of cutoff (6.25 ng/10 mg hair)	6.27	0.25	4.00	6.15	6.30
+50% of cutoff (7.5 ng/10 mg hair)	7.22	0.26	3.91	7.09	7.36

4. Precision for MDMA

a. Within-Run

The intra-assay analytical precision around the cut-off (5 ng/10 mg hair) was determined. 20 replicate hair samples each were spiked before digestion at + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration of 5 ng MDMA per 10 mg hair.

Intra-Assay Precision of the Device

MDMA spiked Concentration	Mean (ng/10 mg hair)	SD (ng/10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/10 mg hair)	3.19	0.20	6.36	3.09	3.28
-25% of cutoff (3.75 ng/10 mg hair)	5.29	0.12	2.31	5.23	5.34
100% of cutoff (5.0 ng/10 mg hair)	6.47	0.27	4.25	6.34	6.59
+25% of cutoff (6.25 ng/10 mg hair)	8.05	0.35	4.36	7.88	8.21
+50% of cutoff (7.5 ng/10 mg hair)	9.77	0.28	2.89	9.65	9.95

b. Between-Run

Inter-assay precision around the cut-off concentration was determined among 20 different assays performed (2 per day) for 10 days. Prior to digestion, hair samples were spiked at each concentration of + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration (5 ng MDMA /10 mg hair).

Inter-Assay Precision of Device

MDMA Concentration	Mean (ng/10 mg hair)	SD (ng/10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/10 mg hair)	3.14	0.18	5.84	3.06	3.23
-25% of cutoff (3.75 ng/10 mg hair)	4.83	0.32	6.64	4.68	4.96
100% of cutoff (5.0 ng/10 mg hair)	6.62	0.43	6.44	6.42	6.82
+25% of cutoff (6.25 ng/10 mg hair)	8.25	0.38	4.65	8.08	8.43
+50% of cutoff (7.5 ng/10 mg hair)	9.76	0.33	3.37	9.64	9.89

6. Cross Reactivity

Before digestion, hair samples (8 mg each) were spiked with the following compounds listed below. The samples were digested, neutralized, assayed by the device, and the $\%B/B_0$ compared to that of methamphetamine at the cutoff.

Cross-Reactivity of Methamphetamine-Related Drugs under Assay Conditions

Compound	Amount of Related Compound (ng/10 mg hair) Required to Produce a Positive Test at the Cutoff of 5 ng/10 mg hair
d,l-MDMA	3.2
l-methamphetamine	170
d-amphetamine	2500
l-amphetamine	9,000
Chloroamphetamine	1250
Methoxyphetamine	90
Fenfluramine	25
d,l-methoxyamphetamine	85
phentermine	>100,000
d-Ephedrine	6500
l-Ephedrine	1250
Phenylpropanolamine	>2500
d,l-MDA	1200
mephentermine	>2500
metanephrine	>2500
d-Pseudoephedrine	800
MDEA	14
Phenmetrazine	650
Phendimetrazine	>100,000

Before digestion, hair samples (8 mg each) were also spiked with 250, 2500 and 10,000 ng/10 mg hair of the following compounds unrelated to methamphetamine. None of the compounds showed any reactivity at the 10,000 ng/10 mg hair level:
Barbital, 10,11-dihydrocarbamezepine, Ethosuximide, mephenytoin, metharbital, 4-methylprimidone, methsuximide, PEMA, phensuximide,carbamazepine, 5,5-diphenylhydantoin, ethotoin, mephobarbital, methyl PEMA, α-methyl- α-propylsuccinimide, N-Normethsuximide, Phenobarbital, primidone, codeine, meperidine, morphine, ethylmorphine, methadone, hydromorphone, oxycodone, diacetylmorphine, chlorpromazine, flurazepam, methaqualone, diazepam, glutethimide, amobarbital, hexobarbital, secobarbital, butabarbital, medazepam, lorazepam, temazepam, oxazepam, diazepam, bromazepam, ethosuximide, normethsuximide, mephenytoin, pheniramine, orphenadrine, chlorpheniramine, promethazine, doxylamine, methapyraline, diphenylpyraline, trimipramine, amitriptyline, nordoxepin, desipramine, doxepin, imipramine, nortriptyline, protriptyline, benzocaine, acetaminophen, buproprion, caffeine, l-cotinine, haloperidol, lidocaine, mepivacaine, ibuprofen, naproxin, phenylpropanolamine, procaine, d-pseudoephedrine, theophylline, nicotine, cocaine, glutethimide, EDDP.

The same un-related compounds tested for cross reactivity were also tested for interference. None of the compounds tested revealed an interference effect on the assay.

7. Analytical Performance of The Device

Analytical performance of the device was calculated using the data of 99 negative samples, 24 negative samples just below the cutoff, and 1505 low positive samples, and 1710 higher concentration samples. The results are

normalized to the workplace population and represented in the table below as per 10,000 samples.

Analytical Performance of The Device

RIA	LC/MS/MS Positive	LC/MS/MS Negative
Positive	107	71
Negative	12	9810

8. Stability of the Radioactive Tracer and Antibody Solutions

The stabilities of the prepared first (methamphetamine-specific) and second (donkey anti-sheep) antibody reagents were tested by comparing various parameters at the time of preparation and after one month of the reagents being in use. The Bo/T x 100, the NSB (as B/Bo x 100) and the B/Bo x 100 depressions of the standards over the range of the curve were compared. The responses did not change over the one-month use and storage conditions.

The stability of the ^{125}I-labeled-methamphetamine tracer used in the methamphetamine assay was assessed by comparing the B/Bo x 100 responses of the calibrators and NSB (nonspecific binding) tube and the Bo/T x 100 of the Zero calibrator with fresh and one month old reagent. These indicators did not change with aging of the prepared tracer.

X. Confirmation of Presumptive Positive Samples

Screen positive samples from the device are confirmed by first weighing out a new portion of the sample (approximately 12 mg), washing, analyzing the wash by RIA and digesting the hair at pH 6.65. Digested samples are extracted and prepared for subsequent analysis by LC/MS/MS for methamphetamine, amphetamine, MDMA and MDA. Positive samples are those with a methamphetamine or MDMA level of 5 ng/10 mg hair or greater after subtraction of 3.5 times the last wash value, and consideration of any appropriate metabolite criteria.

To test the efficacy of the wash procedures, 30 methamphetamine-negative samples were contaminated with methamphetamine by the most severe method of soaking in a concentrated solution of methamphetamine. These samples were then washed for 15 minutes at 37°C with dry isopropanol, then three times for 30 minutes and twice for 60 minutes in phosphate buffer (.01 M, pH 6.0) containing 0.1% albumin. The hair was then digested. The methamphetamine content of the washes and the digest was determined by RIA. After application of the wash kinetic criteria (subtraction of 3.5 times the drug content of the 5th wash from the digest value), all contaminated samples were below the cut-off value of 5 ng/10 mg hair.

In an experiment to test the effects of sweat on drug-contaminated hair, methamphetamine was deposited on 10 different hair samples, and kept moist with a simulated sweat solution for 6 hours. After washing by the standard 3.75 hour wash procedure, the methamphetamine in all 10 samples fell below the 5 ng/10 mg hair cut-off after the standard wash kinetic criteria was applied. The same wash procedure as that applied to the contaminated samples was applied to 39 positive samples from a known user population. All of these samples, after the subtraction of 3.5 times the 5th wash, remained above the cut-off level.

21 samples first analyzed in November 1999 were re-analyzed after having been stored in the collection packets at ambient temperatures until November 2000. The methamphetamine content of the hair samples did not change significantly during one year of storage [Pearson correlation coefficient=0.946].

XI. Percentage Agreement Studies

1. Positive & Negative Percent Agreement

45 drug-using subjects from four rehabilitation clinics with GC/MS-confirmed methamphetamine-positive urines contributed head hair samples. All subjects had positive hair screening results. 40 of the screening-positive hair samples were carried forward to confirmation. Thirty nine (39) samples were confirmed above the cutoff level by LC/MS/MS.

Each of 73 individuals contributed 2 urines per week for 5 weeks, followed by hair collection one week

following the last urine collection. All urines were tested for methamphetamine by EMIT and GC/MS and found to be negative. All hair samples were negative for methamphetamine, with one sample showing the presence of a small amount of methamphetamine below the cut-off level.

Hair Analysis	Urine Analysis Positive	Urine Analysis Negative
Positive	39	0
Negative	1	73

Positive Percent Agreement for RIA Screening Assay = 40/40 = 100%
[95% confidence intervals:]

Positive Percent Agreement for Hair Analysis relative to Urine = 39/(39 + 1) = 97.5%
[95% confidence intervals:]

Negative Percent Agreement = 73/(73 + 0) = 100%
[95% confidence intervals:]

2. Body Hair

Five (5) of the drug-using subjects provided 13 body hair samples and 19 of the individual negative subjects donated 45 body hair samples at the time of the head hair collection. The body hair sites sampled were chest, underarm, and/or leg. All body hair samples from the drug user study agreed with the head hair samples. All negative study body hair samples agreed with the negative head hair samples.

<end>
Submitted 26 October 2001/TCairns

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JAN 2 4 2002

Mr. William R. Thistle, JD
Vice President, General Counsel
Psychemedics Corporation
1280 Massachusetts Avenue, Suite 200
Cambridge, MA 02138

Re: k011185
Trade/Device Name: Psychemedics RIA Methamphetamine and MDMA Assay
Regulation Number: 21 CFR 862.3610
Regulation Name: Methamphetamine Test System
Regulatory Class: Class II
Product Code: DJC
Dated: October 26, 2001
Received: October 29, 2001

Dear Mr. Thistle:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

STATEMENT OF INDICATIONS FOR USE

510(K) Number (if known): K011185

Device Name: **Psychemedics RIA Methamphetamine and MDMA Assay**

Indications for Use:

The Psychemedics Methamphetamine and MDMA Assay is a radioimmunoassay (RIA) for the preliminary qualitative and semi-quantitative detection of d-methamphetamine, d,l-MDMA and metabolites in human hair samples using a 5 ng/10 mg hair cutoff for the purpose of identifying methamphetamine or MDMA (Ecstasy) use. For a quantitative analytical result or to confirm positive results via the presence of methamphetamine, MDMA and metabolites, a more specific alternate chemical method must be used in order to obtain a confirmed analytical result.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K011185

Prescription Use ✓ **OR** **Over-the-Counter Use** _____
(Per 21 CFR 801.109)